Office Action Summary	Application No.	Applicant(s)	
	10/532,067	SUTTER ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-18,20-22,25 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 6-18, and 20-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/23/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Art Examiner to whom the case has been docketed in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Zachariah Lucas in Art Unit 1648.

2. Claims 1, 2, 6-18, 20-22, 25, and 26 are pending and under consideration n the application.

3. In the prior action, mailed on July 21, 2009, claims 1, 2, and 6-25 were pending and rejected.

4. In the response of November 23, 2009, the Applicant amended claims 1, 6, 8-11, 14, 16, 17, 22, and 25; cancelled claims 19, 23, and 24; and added new claim 26.

5. In view of the new and restated grounds of rejection, the action is made Non-Final.

Information Disclosure Statement

6. The information disclosure statement (IDS) submitted on November 23, 2009 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Specification

7. **(New Objection)** The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Applicant is requested to insert antecedent basis support

(acknowledging that written description support is present) for the claim limitation regarding vaccines which "do not comprise an adjuvant."

Claim Objections

8. **(Prior Objection- Withdrawn)** Claim 19 was objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. In view of the cancellation of the claim, the objection is withdrawn.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. **(Prior Rejection- Withdrawn)** Claims 1, 2, and 6-25 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant's arguments in traversal are found persuasive. The rejection is therefore withdrawn.

11. **(New Rejection)** Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim is directed to a the MVA of claim 1, comprising a signal sequence that controls the glycosylphosphatidylinositol (GPI) anchoring of the protein to a cell surface. It is noted that the teachings in the art indicate that such a signal sequence is required for the protein to be so attached to a cell membrane. See e.g., Yang et al., Glycobiology

9:1347-56, at page 1352 (right column – indicating that MSP-1 proteins lacking the signal sequence are not found on the cell membrane). However, this reference indicates that the N-terminal signal sequence is not the sole sequence required. The reference indicates that, in addition to the 5' (N-terminal) signal sequence an additional C-terminal GPI anchor (GA) signal sequence is also required. Id. Further, each of Figure 1 in the present application and Figure 6 of the Kauth reference cited on page 12 of applicant's November 2009 Response indicate that this GA signal sequence is not a part of the p42 sequence. Thus, it is not clear if claim 10 is suggesting that the signal sequence alone is capable of causing the GPI anchoring of the protein, if the claim is merely requiring that the signal sequence would permit GPI anchoring if the GA was present, or if the claim is intended to implicitly require the presence of a GA signal sequence at the C-terminal of the encoded protein in addition to the explicitly referenced N-terminal (5') signal sequence.

12. **(New Rejection)** Claims 14 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 14 is drawn to a vaccine comprising a) the recombinant MVA of claim 1, and one of the antigenic compounds identified in claim 14 as component c) of the claimed vaccine. Claim 15 indicates that the components a) (the MVA vector) and c) (the additional antigenic component of claim 14) may be administered simultaneously, sequentially, or separately. If the compounds are part of the same vaccine composition, it is not clear how they can be administered sequentially or separately. Thus, it is not clear what is being claimed. I.e., it is not clear if claim 14 is requiring the presence of

components a) and c) in the same composition (as it appears to do on its face) or if the claim is intended to be drawn to a vaccination kit comprising in separate compartments the components of a) and c) as the limitations of claim 15 imply.

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. **(Prior Rejection- Withdrawn)** Claims 20 and 22-25 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (i.e. as incorporating New Matter to the application) with respect to the vaccines that do not comprise an adjuvant. Applicant's arguments in traversal are found persuasive. The rejection is therefore withdrawn.

15. **(Prior Rejection- Withdrawn)** Claims 13-25 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement with respect to vaccines comprising any fragment of mutein of a *Plasmodium falciparum* MSP-1 protein. In view of the amendments to the claim, the rejection is withdrawn.

16. **(Prior Rejection- Withdrawn)** Claims 13-25 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the MSP-1 protein of *Plasmodium falciparum*, does not reasonably provide enablement for all fragments and muteins of MSP-1 and all MSP-1 with reduced AT content. In view of the amendments to the claim, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. **(Prior Rejection- Restated)** Claims 1-2 and 6-21 were rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Schneider et al. (Nature Medicine, 1998, Vol. 4, No. 4, pages 397-402) in view of Yang et al. (Vaccine, 1997, Vol. 15, No. 12/13, pages 1303-1313), Kumar et al. (Immunology Letters, April 2002, Vol. 81, pages 13-24) and Bujard et al. (WO 98/14583, 1998).

The rejection is withdrawn from cancelled claim 19.

It is noted that the claim limitation requiring the additional teachings of Sedegah et al. have been deleted from claims 22-25. The present rejection is therefore extended to amended claims 22-25. With respect to claim 20, requiring the absence of an adjuvant in a vaccine comprising the MVA vector, it is noted that

It is noted that the statement of the rejection, particularly on page 12 of the prior action, indicated that the teachings of the prior art would have rendered obvious the production of a DNA vaccine, and particularly a plasmid DNA vaccine, expressing the *P. falciparum* p42 antigen.

The teachings of the reference were described previously.

As was previously described, the present claims are drawn to recombinant modified vaccinia virus Ankara vectors encoding the p42 fragment of MSP-1, particularly from the isolate 3D7, and to methods for the production of the vector, and the use of the vector as a vaccine against malaria. The conclusion indicated in the prior action, was that the cited art rendered obvious the construction and use of plasmid DNA encoding the p42 fragment. This is accurate.

However, the teachings of the prior art also render obvious the construction of MVA vectors encoding the p42 fragment (and the other fragments identified in the cited art) as a booster vaccine for the plasmid DNA vaccines.

This is because, each of the Kumar and Schneider references teach the use of vaccinia virus vectors as effective boosters for prior primary administrations of other anti-malarial vaccines. While, as noted by the Applicant, Schneider indicates that MVA may or may not be an effective primary composition, the teachings in the art provide those of ordinary skill in the art with a reasonable expectation of success in the use of the MVA as a booster vaccine. Such teachings find additional support in the art. For example, Zavala et al. (Virology, 280:155-59, at 157-58) indicates that vaccinia virus vectors, and particularly MVA, are particularly effective booster vaccine compositions. Thus, while the teachings of Schneider provide evidence that it may not have been obvious (on the basis of unpredictability) to use the claimed MVA vectors in a primary vaccination, the teachings of the art indicate that the converse is true with respect to its use as a booster composition.

Applicant's assertion that Kumar only teaches the administration of the MVA to cells for CTL analysis is noted. Nonetheless, the reference does teach the use of viral vectors for the purpose of boosting a primary administration of different antigenic composition, such as a

plasmid vaccine. Pages 14 (right column) and 23. This argument by the Applicant is therefore not found persuasive.

From the teachings of these references, it would have been obvious to those of ordinary skill in the art to use p42 antigen identified as a protective antigen in Kumar as the encoded antigen in the plasmid DNA priming/MVA boosting technique suggested by the teachings of Kumar and Schneider.

In view of the above, the Applicant's arguments on page 14 if the Response, asserting unpredictability and that Schneider teaches away from the claimed invention, are not found persuasive.

The additional arguments presented in the Response each assert deficiencies in the individual applied references. It is established in the patent law that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See e.g., *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). These remaining arguments are therefore not found persuasive.

It is noted that the teachings of Bujard are applied primarily to render obvious the claim limitations requiring the reduced adenine and thymine content of the MSP-1 fragment coding sequences, now found only in claims 25 and 26. As the reference teaches the application of such a method to the production of *Plasmodium* vaccines, such as live vaccinia virus based vaccines (see e.g., column 8, of U.S. 6,933,130- the U.S. national stage of the Bujard reference), it would

have been obvious to those of ordinary skill in the art to apply the stabilization method of that reference to the p42 coding sequences in the plasmids and MVA vectors suggested by Schneider and Kumar.

Similarly, the teachings of Yang primarily render obvious the inclusion of the signal sequences referred to in claims 6-10. In particular, the reference teaches that the inclusion of such signal sequences in vaccinia vectors encoding the MSP-1 antigens of the reference resulted in the surface expression of the antigens on the infected cells, which resulted in an enhanced response against the antigens. Thus, it would have been obvious to those of ordinary skill in the art to have used this technique to enhance the immunogenicity of the antigens encoded by the MVA vectors of Schneider. This is particularly the case when the teachings of Langford et al. (Molec Cell Biol 6:3191-99- cited on page 1311 of Yang) are considered. This reference indicates that the surface expression through the inclusion of signal sequences in antigens expression by live virus vectors generally results in increased immunogenicity. Thus, those ordinary skill in the art would have had a reasonable expectation of success in the application of this immunogenicity enhancing method to the vectors suggested by Schneider and Kumar.

In addition to the teachings previously described, it is also noted that the vaccinia vector described by Kumar includes a selection marker, and that this selection marker was accepted in the art as also useful in the vaccinia MVA vector. See e.g., Staib et al., Biotechniques 28:1137. Thus, it would have been obvious to those of ordinary skill in the art to have used this selection marker in the vaccinia MVA vector of Schneider as a means for selecting MVA properly incorporating the MSP-1 coding sequence.

For the reasons above and of record, and in view of the above re-characterization of the rejection, the Applicant's arguments are not found persuasive, and the rejection is maintained.

19. **(Prior Rejection- Withdrawn)** Claims 22-25 were rejected under 35 U.S.C. 103(a) as being unpatentable over Schneider et al., Yang et al., Kumar et al., and Bujard et al. as applied against claims 1, 2, and 6-21; and further in view of Sedegah et al. (PNAS, 1994, Vol. 91, No. 21, pages 9866-9870). In view of the amendment of the claims, and extension of the above rejection to claims 22-25, this rejection is withdrawn.

20. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Double Patenting

21. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

22. **(New Rejection)** Claims 1, 2, 6-18, and 20-25 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 12-19, and 23-31 of U.S. Patent No. 7,198,934, or of claims 1-5, 8-11, 16-19, 24-28, 31, and 33 of US Patent 6,440,422; in view of the teachings of Schneider et al., Yang et al., Kumar et al., Bujard et al., and Sedegah et al. as applied above. The patented claims are generic to the present claims, and fail to specify the use of the MSP-1 fragments, the signal sequences, and the inclusion or co-administration of the additional antigenic agents. however, such limitations would have been obvious based on the teachings of the secondary references as described above and previously. The present claims therefore represent an obvious embodiment of the patented claims.

23. **(New Rejection)** Claims 11, 12, and 18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 12-19, and 23-31 of U.S. Patent No. 7,049,145 in view of the teachings of Schneider et al. and Kumar et al. as applied above. The patent claims are generic to the present claims. However, the missing limitations would have been obvious to those of ordinary skill in the art based on the teachings of

the Schneider and Kumar as described above. The present claims therefore represent obvious variations from the patented claims.

24. **(New Rejection)** Claims 1, 2, 6-18, and 20-25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5, 7, 11, and 12 of copending Application No. 11/375,159 in view of in view of the teachings of Schneider et al., Yang et al., Kumar et al., Bujard et al., and Sedegah et al. as applied above. The copending claims read on recombinant MVA encoding plasmodium antigens. However, the reference does not identify the specific antigens of the present claims, or the signal sequences, and the inclusion or co-administration of the additional antigenic agents. however, such limitations would have been obvious based on the teachings of the secondary references as described above and previously. The present claims therefore represent obvious variations from the copending claims.

This is a provisional obviousness-type double patenting rejection.

25. Claims 1, 2, and 6-25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5, 7, 11, and 12 of copending Application No. 11/375,159 in view of in view of the teachings of Schneider et al., Yang et al., Kumar et al., Bujard et al., and Sedegah et al. as applied above. The copending claims read on recombinant MVA encoding plasmodium antigens. However, the reference does not identify the specific antigens of the present claims, or the signal sequences, and the inclusion or co-administration of the additional antigenic agents. however, such limitations would have

been obvious based on the teachings of the secondary references as described above and previously. The present claims therefore represent obvious variations from the copending claims.

This is a provisional obviousness-type double patenting rejection.

26. Claim 17 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 and 21-24 of copending Application No. 12/523023 in view of in view of the teachings of Schneider et al., Yang et al., Kumar et al., Bujard et al., and Sedegah et al. as applied above. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims read on a method of using the products of the copending application, wherein at least the use of the products as vaccines are taught by the copending specification and claims. The additional limitations of the present claims would have been obvious in view of the teachings of the secondary references as described above.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

This rejection is necessitated by the decision of the Court of Appeals for the Federal Circuit in Pfizer Inc. v Teva pharmaceuticals USA Inc., 86 USPQ2d 1001, at page 1008 (March 2008), which indicates that there is no patentable distinction between claims to a product and a method of using that product disclosed in the specification of the application and that the preclusion of such a double patenting rejection under 35 USC 121 does not apply where the present application is other than a divisional application of the patent application containing such patentably indistinct claims.

Conclusion

27. No claims are allowed.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is (571)272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick J. Nolan can be reached on 571-272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachariah Lucas/
Primary Examiner, Art Unit 1648